LAMICTAL Monotherapy NDA
(Data as of:)

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Table 6.18
Overall Incidence of Treatment Emergent Adverse Experiences
on Add-on and Monotherapy LAMICTAL Treatment in Completed Monotherapy Studies

Body System	Preferred Adverse Experience Term	LAMICTAL Patients (N=868) Patients No.	Patients % [1]	Number of Patients with Maximum Intensity[2] Mild	Moderate	Severe
	OCCLUS RETINAL ART	1	0.1%		0	
	OTITIS MED	1	0.1%		0	
	PAROSMIA	1	0.1%		0	
	PHOTOPHOBIA	1	0.1%		0	
	STRABISMUS	1	0.1%		0	
	TINNITUS	1	0.1%		0	
	UVEITIS	1	0.1%		0	
	VISUAL FIELD DEFECT	1	0.1%		0	
Urogenital	INFECT URIN TRACT	6	0.7%		5	
	CYSTITIS	4	0.5%		2	
	HEMATURIA	2	0.2%		1	
	DYSURIA	1	0.1%		0	
	KIDNEY FUNC ABNORM	1	0.1%		0	
	POLYURIA	1	0.1%		0	
	URIN ABNORM	1	0.1%		0	
	URIN FREQUENCY	1	0.1%		0	
	URIN IMPAIRED	1	0.1%		1	
	URIN RETENT	1	0.1%		0	
	URIN TRACT DISORDER	1	0.1%		0	
	URIN URGENCY	1	0.1%		0	
Urogenital (Female)	DYSMENORRHEA	10	2.2%		3	
	MENS DISORDER	10	2.2%		1	
	ABORTION	1	0.2%		1	
	AMENORRHEA	1	0.2%		0	
	HEMORR UTER	1	0.2%		1	
	LACTATION FEM	1	0.2%		1	
	METRORRHAGIA	1	0.2%		0	
	PAIN BREAST	1	0.2%		0	
	PREGN UNINTEND	1	0.2%		0	
	UTER FIBROID ENLARGE	1	0.2%		0	
	VAGINITIS	1	0.2%		0	
	VULVOVAGINAL DISORDER	1	0.2%		0	

[1]Percentage is calculated using the overall number of LAMICTAL patients (N=868) as the denominator for all the AEs except for sex specific AEs. Appropriate denominator was used for sex specific AEs. (N=415 and N=453 for male and female, respectively.)

[2]Intensity classification was occasionally missing.

The term ALL RASH includes the following COSTART terms: RASH, RASH PUST, RASH MAC PAP, URTICARIA, STEVENS JOHNSON SYND and RASH VESIC BULL.

Table 6.18
Overall Incidence of Treatment Emergent Adverse Experiences
on Add-on and Monotherapy LAMICTAL Treatment in Completed Monotherapy Studies

Body System	Preferred Adverse Experience Term	LAMICTAL Patients (N=868)				
		Patients		Number of Patients with Maximum Intensity[2]		
		No.	% [1]	Mild	Moderate	Severe
Urogenital (Male)	IMPOTENCE	1	0.2%		0	
	PROSTAT DISORDER	1	0.2%		0	

[1]Percentage is calculated using the overall number of LAMICTAL patients (N=868) as the denominator for all the AEs except for sex specific AEs. Appropriate denominator was used for sex specific AEs. (N=415 and N=453 for male and female, respectively.)

[2]Intensity classification was occasionally missing.

The term ALL RASH includes the following COSTART terms: RASH, RASH PUST, RASH MAC PAP, URTICARIA, STEVENS JOHNSON SYND and RASH VESIC BULL.

Table 6.22

Incidence of Serious/Life Threatening Adverse Experiences[1] on LAMICTAL in Completed Monotherapy Studies (Add-on and Monotherapy Treatment Combined)

Body System	Preferred Adverse Experience Term	LAMICTAL Patients (N=868)				
		Patients		Number of Patients with Maximum Intensity[3]		
		No.	%[2]	Mild	Moderate	Severe
Total No. of Patients with Serious/Life Threatening AE		47	5.4%			
General	REACT AGGRAV	9	1.0%		5	
	REACT UNEVAL	4	0.5%		0	
	HEADACHE	3	0.3%		1	
	NEOPL	2	0.2%		0	
	PAIN	2	0.2%		1	
	ALLERG REACT	1	0.1%		1	
	FEVER	1	0.1%		0	
	INFECT	1	0.1%		1	
	INJURY ACCID	1	0.1%		0	
	PAIN CHEST	1	0.1%		1	
Cardiovascular	CEREBROVASC ACCI	1	0.1%		1	
	EMBOL CEREBR	1	0.1%		1	
	FIBRILLAT ATR	1	0.1%		1	
	INFARCT CEREBR	1	0.1%		1	
	INFARCT MYOCARD	1	0.1%		0	
Digestive	HEMATEMESIS	2	0.2%		2	
	VOMIT	2	0.2%		0	
	NAUSEA	1	0.1%		1	
	ULCER STOMACH	1	0.1%		1	
Hemic & Lymphatic	ANEMIA	1	0.1%		1	
Nervous System	CONFUS	2	0.2%		0	
	DIZZINESS	2	0.2%		1	
	HEMIPLEGIA	2	0.2%		2	
	NEOPL CNS	2	0.2%		0	
	ATAXIA	1	0.1%		1	
	DEPRESSION	1	0.1%		0	
	HOSTILITY	1	0.1%		1	
	PARESTHESIA	1	0.1%		1	

[1]Includes both treatment emergent and non-treatment emergent AEs.

[2]Percentage is calculated using the overall number of LAMICTAL patients (868) as the denominator except for sex specific AEs. Appropriate denominator was used for sex specific AEs (N=415 and N=453 for male and female, respectively.).

[3]Intensity classification was occasionally missing.

Table 6.22

Incidence of Serious/Life Threatening Adverse Experiences[1] on LAMICTAL in Completed Monotherapy Studies (Add-on and Monotherapy Treatment Combined)

Body System	Preferred Adverse Experience Term	LAMICTAL Patients (N=868)				
		Patients		Number of Patients with Maximum Intensity[3]		
		No.	% [2]	Mild	Moderate	Severe
	PERSON DISORDER	1	0.1%		1	
	PSYCHOSIS	1	0.1%		0	
	SUICIDAL IDEATIO	1	0.1%		0	
	VERTIGO	1	0.1%		0	
Respiratory	DYSPNEA	2	0.2%		2	
Skin	ALL RASH	8	0.9%		4	
	RASH	6	0.7%		3	
	PRURITUS	1	0.1%		1	
	RASH MAC PAP	1	0.1%		1	
	STEVENS JOHNSON	1	0.1%		0	
Special Senses	DEAF TRANS	1	0.1%		0	
	DIPLOPIA	1	0.1%		0	
	OCCLUS RETINAL A	1	0.1%		0	
	PHOTOPHOBIA	1	0.1%		0	
Urogenital	ABORTION	1	0.2%		1	
	HEMORR UTER	1	0.2%		1	
	HEMATURIA	1	0.1%		1	
	KIDNEY FAIL	1	0.1%		0	

[1]Includes both treatment emergent and non-treatment emergent AEs.

[2]Percentage is calculated using the overall number of LAMICTAL patients (868) as the denominator except for sex specific AEs. Appropriate denominator was used for sex specific AEs (N=415 and N=453 for male and female, respectively.).

[3]Intensity classification was occasionally missing.

Table 6.22.1. Listing of All LAMICTAL Patients with Serious/Life Threatening Adverse Experiences[a] not Listed on Table 6.22

Primary Study Sdy–Ctr–Pt	Current Study Sdy–Ctr–Pt	Age/ Sex	RAW ADVERSE EXPERIENCE TERM	AE Onset Phase[b]	Total Daily Dose Prior to Onset (mg/day)	Duration of Dose at Onset Days	Attributable to Study Drug?	Withdrawal due to AE?
89–1–112	89–1–112	38/F	MENINGIOMA	Post–Study	NA	NA	UNK	NA
105–1–11403	105–1–11043	41/F	SUDDEN UNEXPLAINED DEATH	Mono	UNK	300	UNK	YES
105–1–9411	105–1–9411	23/F	INC SEIZURE FREQUENCY	Add–on	UNK	UNK	Yes	No
105–3202	112–23–3202	34/F	FALLOPIAN TUBE LIGATURE	Cont	450	784	No	No
105–3206	112–32–3206	20/M	ACCIDENTAL FRACTURE OF LEFT SHOULDER BLADE	Cont	400	669	No	No
105–3603	112–36–3603	23/F	HOSPITALIZATION FOR VIDEO EEG STUDY DUE TO MARKED DETERIORATION	Cont	300	535	No	No
105–3803	112–38–3803	19/M	HOSPITALIZATION DUE TO DISCOVERY OF TEMPORAL OCCIPITAL LESION ON MRI SCAN	Cont	500	758	No	No
105–5204	112–52–5204	30/M	SUDDEN DEATH	Cont	400	355	UNK	Yes
105–9102	112–91–9102	34/M	HOSPITALIZATION FOR IMPLANT OF VAGUS STIMULATOR	Cont	600	659	No	No

[a] Includes both treatment emergent and non–treatment emergent AEs.

[b] Add–on = Add–on period. Mono = Monotherapy Period. Cont = Continuation Study.

LAMICTAL Monotherapy NDA
(Data as of:)

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Table 6.23
Incidence of Serious/Life Threatening Treatment Emergent Adverse Experiences Leading to Discontinuation of LAMICTAL in Completed Monotherapy Studies (Add-on and Monotherapy Treatment Combined)

Body System	Preferred Adverse Experience Term	LAMICTAL Patients (N=868)				
		Patients		Number of Patients with Maximum Intensity[2]		
		No.	% [1]	Mild	Moderate	Severe
Total No. of Patients with Serious/Life Threatening AE Leading to Disc.		19	2.2%			
General	REACT AGGRAV	5	0.6%		1	
	FEVER	1	0.1%		0	
	HEADACHE	1	0.1%		1	
	NEOPL	1	0.1%		0	
	PAIN	1	0.1%		1	
	PAIN CHEST	1	0.1%		1	
Digestive	NAUSEA	1	0.1%		1	
Nervous System	CONFUS	1	0.1%		0	
	DEPRESSION	1	0.1%		0	
	DIZZINESS	1	0.1%		1	
	PARESTHESIA	1	0.1%		1	
	PERSON DISORDER	1	0.1%		1	
	PSYCHOSIS	1	0.1%		0	
Respiratory	DYSPNEA	2	0.2%		2	
Skin	ALL RASH	8	0.9%		4	
	RASH	6	0.7%		3	
	PRURITUS	1	0.1%		1	
	RASH MAC PAP	1	0.1%		1	
	STEVENS JOHNSON	1	0.1%		0	

[2]Percentage is calculated using the overall number of LAMICTAL patients (868) as the denominator.

[3]Intensity classification was occasionally missing.

Table 6.26
Incidence of Adverse Experiences Leading to Discontinuation of LAMICTAL in Completed Monotherapy Studies (Add-on and Monotherapy Treatment Combined)

Body System	Preferred Adverse Experience Term	LAMICTAL Patients (N=868) Patients No.	Patients % [1]	Number of Patients with Maximum Intensity [2] Mild	Moderate	Severe
Total No. of Patients with Discontinuation Due to AEs		116	13.4%			
General	ASTHENIA	13	1.5%		8	
	HEADACHE	9	1.0%		6	
	FEVER	8	0.9%		1	
	REACT AGGRAV	8	0.9%		3	
	PAIN BACK	3	0.3%		0	
	PAIN CHEST	3	0.3%		1	
	REACT UNEVAL	3	0.3%		1	
	PAIN	2	0.2%		1	
	FLU SYND	1	0.1%		0	
	IMMUNE SYSTEM DI	1	0.1%		0	
	INFECT	1	0.1%		1	
	LAB TEST ABNORM	1	0.1%		1	
	MALAISE	1	0.1%		1	
	NEOPL	1	0.1%		0	
	NO DRUG EFFECT	1	0.1%		0	
	PAIN NECK	1	0.1%		1	
Cardiovascular	PALPITAT	2	0.2%		1	
	VASODILAT	2	0.2%		0	
	MIGRAINE	1	0.1%		1	
Digestive	NAUSEA	8	0.9%		6	
	VOMIT	4	0.5%		2	
	DIARRHEA	2	0.2%		0	
	DYSPEPSIA	2	0.2%		1	
	DRY MOUTH	1	0.1%		1	
	DYSPHAGIA	1	0.1%		0	
	GASTROENTERITIS	1	0.1%		0	
	HYPER GUM	1	0.1%		1	
	TOOTH DISORDER	1	0.1%		0	
Hemic & Lymphatic	LYMPHADENO	5	0.6%		2	

[2]Percentage is calculated using the overall number of LAMICTAL patients (868) as the denominator.

[3]Intensity classification was occasionally missing.

LAMICTAL Monotherapy NDA
(Data as of:)

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Table 6.26
Incidence of Adverse Experiences Leading to Discontinuation of LAMICTAL in Completed Monotherapy Studies (Add-on and Monotherapy Treatment Combined)

Body System	Preferred Adverse Experience Term	LAMICTAL Patients (N=868)				
		Patients		Number of Patients with Maximum Intensity[2]		
		No.	% [1]	Mild	Moderate	Severe
	ANEMIA	1	0.1%		1	
	ECCHYMOSIS	1	0.1%		0	
	LEUKOCYTOSIS	1	0.1%		0	
	LEUKOPENIA	1	0.1%		0	
	RBC ABNORM	1	0.1%		1	
	THROMBOCYTOPENIA	1	0.1%		0	
Metabolic & Nutritional	EDEMA	2	0.2%		1	
	SGOT INC	2	0.2%		1	
	SGPT INC	1	0.1%		0	
	WEIGHT INC	1	0.1%		0	
Musculoskeletal	ARTHRALGIA	2	0.2%		2	
	CRAMPS LEG	1	0.1%		0	
	MYALGIA	1	0.1%		0	
Nervous System	DIZZINESS	12	1.4%		5	
	ANXIETY	5	0.6%		3	
	INSOMNIA	5	0.6%		1	
	SOMNOLENCE	5	0.6%		2	
	AMNESIA	4	0.5%		2	
	VERTIGO	4	0.5%		1	
	PARESTHESIA	3	0.3%		1	
	PERSON DISORDER	3	0.3%		1	
	CONFUS	2	0.2%		1	
	NERVOUSNESS	2	0.2%		1	
	AKATHISIA	1	0.1%		1	
	ATAXIA	1	0.1%		0	
	DEPRESSION	1	0.1%		0	
	EMOTION LABIL	1	0.1%		1	
	HOSTILITY	1	0.1%		0	
	HYPERKINESIA	1	0.1%		1	
	HYPOTONIA	1	0.1%		0	
	PSYCHOSIS	1	0.1%		0	
	SPEECH DISORDER	1	0.1%		0	

[2]Percentage is calculated using the overall number of LAMICTAL patients (868) as the denominator.

[3]Intensity classification was occasionally missing.

Table 6.26
Incidence of Adverse Experiences Leading to Discontinuation of LAMICTAL in Completed Monotherapy Studies (Add-on and Monotherapy Treatment Combined)

Body System	Preferred Adverse Experience Term	LAMICTAL Patients (N=868)				
		Patients		Number of Patients with Maximum Intensity[2]		
		No.	% [1]	Mild	Moderate	Severe
	TREMOR	1	0.1%		0	
Respiratory	PHARYNGITIS	3	0.3%		2	
	DYSPNEA	2	0.2%		2	
	BRONCHITIS	1	0.1%		1	
	COUGH INC	1	0.1%		0	
Skin	ALL RASH	53	6.1%		29	
	RASH	43	5.0%		25	
	PRURITUS	7	0.8%		4	
	RASH MAC PAP	7	0.8%		4	
	SWEAT	2	0.2%		0	
	URTICARIA	2	0.2%		0	
	ALOPECIA	1	0.1%		0	
	STEVENS JOHNSON	1	0.1%		0	
Special Senses	DIPLOPIA	9	1.0%		4	
	AMBLYOPIA	1	0.1%		1	
	CONJUNCTIVITIS	1	0.1%		1	
	HYPERACUSIS	1	0.1%		0	
	TASTE PERVERS	1	0.1%		0	

[2]Percentage is calculated using the overall number of LAMICTAL patients (868) as the denominator.

[3]Intensity classification was occasionally missing.

Table 6.27
Incidence of Adverse Experiences Leading to Discontinuation
in Study 30/31 (Add-on and Monotherapy Treatment Combined)

Body System Adverse Experience[1]	LAMICTAL (N=76) No. (%) of Pts	LAMICTAL (N=76) No. of Pts. with Maximum Intensity: Mild	Mod	Sev	VPA (N=80) No. (%) of Pts	VPA (N=80) No. of Pts. with Maximum Intensity: Mild	Mod	Sev
Number of Patients with AE Leading to Disc.	15 (20)				6 (8)			
General								
FEVER	2 (3)		0		0 (0)		0	
ASTHENIA	1 (1)		0		0 (0)		0	
HEADACHE	1 (1)		1		1 (1)		1	
PAIN	1 (1)		1		0 (0)		0	
PAIN CHEST	1 (1)		1		0 (0)		0	
PAIN NECK	1 (1)		1		0 (0)		0	
REACT AGGRAV	0 (0)		0		1 (1)		0	
Digestive								
DIARRHEA	1 (1)		0		0 (0)		0	
NAUSEA	1 (1)		1		0 (0)		0	
VOMIT	1 (1)		1		0 (0)		0	
DYSPEPSIA	0 (0)		0		1 (1)		0	
HEPATITIS	0 (0)		0		1 (1)		0	
Hemic & Lymphatic								
LYMPHADENO	2 (3)		2		0 (0)		0	
Metabolic & Nutritional								
WEIGHT INC	1 (1)		0		0 (0)		0	
Musculoskeletal								
CRAMPS LEG	1 (1)		0		0 (0)		0	
MYALGIA	1 (1)		0		0 (0)		0	
Nervous System								
DIZZINESS	3 (4)		2		1 (1)		1	
ANXIETY	2 (3)		0		1 (1)		1	
ATAXIA	1 (1)		0		0 (0)		0	
PERSON DISORDER	1 (1)		1		0 (0)		0	
TREMOR	1 (1)		0		0 (0)		0	

[1]The term ALL RASH includes the following COSTART terms: RASH, RASH PUST, RASH MAC PAP, URTICARIA, STEVENS JOHNSON SYND and RASH VESIC BULL.

Table 6.27
Incidence of Adverse Experiences Leading to Discontinuation in Study 30/31 (Add-on and Monotherapy Treatment Combined)

Body System Adverse Experience[1]	LAMICTAL (N=76) No. (%) of Pts	No. of Pts. with Maximum Intensity Mild	Mod	Sev	VPA (N=80) No. (%) of Pts	No. of Pts. with Maximum Intensity Mild	Mod	Sev
CONVULS GRAND MAL	0 (0)		0		1 (1)		0	
PARANOID REACT	0 (0)		0		1 (1)		0	
Respiratory								
DYSPNEA	1 (1)		1		0 (0)		0	
Skin								
ALL RASH	6 (8)		3		1 (1)		0	
RASH	3 (4)		2		1 (1)		0	
PRURITUS	2 (3)		1		0 (0)		0	
RASH MAC PAP	2 (3)		1		0 (0)		0	
ALOPECIA	1 (1)		0		0 (0)		0	
STEVENS JOHNSON SYND	1 (1)		0		0 (0)		0	
Special Senses								
DIPLOPIA	2 (3)		0		0 (0)		0	

[1]The term ALL RASH includes the following COSTART terms: RASH, RASH PUST, RASH MAC PAP, URTICARIA, STEVENS JOHNSON SYND and RASH VESIC BULL.

Table 6.28
Incidence of Adverse Experiences Leading to Discontinuation from Monotherapy Studies in Newly Diagnosed Patients (Primary Study of Participation Only)

Body System Adverse Experience[1]	LAMICTAL (N=446) No. (%) of Pts	LAMICTAL No. of Pts. with Maximum Intensity: Mild	Mod	Sev	CBZ (N=247) No. (%) of Pts	CBZ No. of Pts. with Maximum Intensity: Mild	Mod	Sev	PHT (N= 95) No. (%) of Pts	PHT No. of Pts. with Maximum Intensity: Mild	Mod	Sev
Number of Patients with AE Leading to Disc.	42 (9)				47 (19)				17 (17)			
General												
ASTHENIA	5 (1)	3			8 (3)	2			4 (4)	0		
HEADACHE	4 (<1)	4			7 (2)	4			5 (5)	3		
PAIN BACK	3 (<1)	0			0 (0)	0			1 (1)	1		
FEVER	2 (<1)	0			1 (<1)	1			0 (0)	0		
PAIN CHEST	2 (<1)	0			0 (0)	0			0 (0)	0		
FLU SYND	1 (<1)	0			3 (1)	2			0 (0)	0		
INFECT	1 (<1)	1			0 (0)	0			0 (0)	0		
MALAISE	1 (<1)	1			2 (<1)	0			0 (0)	0		
NEOPL	1 (<1)	0			1 (<1)	1			0 (0)	0		
PAIN	1 (<1)	0			0 (0)	0			1 (1)	0		
REACT UNEVAL	1 (<1)	1			1 (<1)	1			1 (1)	0		
PAIN ABDO	0 (0)	0			1 (<1)	0			0 (0)	0		
Cardiovascular												
VASODILAT	2 (<1)	0			1 (<1)	0			0 (0)	0		
MIGRAINE	1 (<1)	1			0 (0)	0			0 (0)	0		
PALPITAT	1 (<1)	0			0 (0)	0			0 (0)	0		
ARRHYTHMIA	0 (0)	0			1 (<1)	1			0 (0)	0		
FIBRILLAT ATR	0 (0)	0			1 (<1)	1			0 (0)	0		
Digestive												
NAUSEA	3 (<1)	3			6 (2)	1			2 (2)	2		
VOMIT	2 (<1)	1			1 (<1)	1			0 (0)	0		
DYSPEPSIA	1 (<1)	1			0 (0)	0			0 (0)	0		
DYSPHAGIA	1 (<1)	0			0 (0)	0			0 (0)	0		
TOOTH DISORDER	1 (<1)	0			0 (0)	0			0 (0)	0		
ANOREXIA	0 (0)	0			1 (<1)	1			0 (0)	0		
DIARRHEA	0 (0)	0			1 (<1)	1			0 (0)	0		
DRY MOUTH	0 (0)	0			1 (<1)	0			0 (0)	0		
LIVER DAMAGE	0 (0)	0			1 (<1)	1			0 (0)	0		

[1]The term ALL RASH includes the following COSTART terms: RASH, RASH PUST, RASH MAC PAP, URTICARIA, STEVENS JOHNSON SYND and RASH VESIC BULL.

Includes adverse event data from studies 49,74,89 and 106 only.

Sex specific AEs used appropriate denominators. (In LTG group, N=228 and N=218 for male and female, respectively. In CBZ group, N=116 and N=131 for male and female, respectively. In PHT group, N= 54 and N= 41 for male and female, respectively.)

Table 6.28
Incidence of Adverse Experiences Leading to Discontinuation from Monotherapy Studies
in Newly Diagnosed Patients (Primary Study of Participation Only)

Body System Adverse Experience[1]	LAMICTAL (N=446) No. (%) of Pts	LAMICTAL No. of Pts. with Maximum Intensity: Mild	Mod	Sev	CBZ (N=247) No. (%) of Pts	CBZ No. of Pts. with Maximum Intensity: Mild	Mod	Sev	PHT (N= 95) No. (%) of Pts	PHT No. of Pts. with Maximum Intensity: Mild	Mod	Sev
Hemic & Lymphatic												
LYMPHADENO	1 (<1)	0			2 (<1)	0			0 (0)	0		
LEUKOPENIA	0 (0)	0			1 (<1)	0			1 (1)	0		
THROMBOCYTOPENIA	0 (0)	0			1 (<1)	0			0 (0)	0		
Metabolic & Nutritional												
SGOT INC	2 (<1)	1			1 (<1)	1			0 (0)	0		
EDEMA	1 (<1)	1			1 (<1)	1			0 (0)	0		
PHOSPHATASE ALK INC	0 (0)	0			1 (<1)	1			0 (0)	0		
SGPT INC	0 (0)	0			3 (1)	2			0 (0)	0		
Musculoskeletal												
ARTHRALGIA	2 (<1)	2			0 (0)	0			0 (0)	0		
MYALGIA	0 (0)	0			1 (<1)	0			0 (0)	0		
Nervous System												
INSOMNIA	3 (<1)	1			1 (<1)	0			1 (1)	0		
AMNESIA	1 (<1)	1			1 (<1)	1			0 (0)	0		
DEPRESSION	1 (<1)	1			0 (0)	0			1 (1)	1		
DIZZINESS	1 (<1)	0			5 (2)	4			0 (0)	0		
EMOTION LABIL	1 (<1)	1			1 (<1)	0			0 (0)	0		
PARESTHESIA	1 (<1)	1			1 (<1)	0			0 (0)	0		
SOMNOLENCE	1 (<1)	0			7 (2)	2			4 (4)	0		
SPEECH DISORDER	1 (<1)	0			0 (0)	0			0 (0)	0		
AKATHISIA	0 (0)	0			1 (<1)	0			0 (0)	0		
ATAXIA	0 (0)	0			4 (1)	2			2 (2)	0		
COORDINAT ABNORM	0 (0)	0			0 (0)	0			1 (1)	0		
HOSTILITY	0 (0)	0			1 (<1)	1			1 (1)	1		
MYOCLONUS	0 (0)	0			1 (<1)	0			0 (0)	0		
NEOPL CNS	0 (0)	0			1 (<1)	0			0 (0)	0		
NERVOUSNESS	0 (0)	0			1 (<1)	1			0 (0)	0		
PERSON DISORDER	0 (0)	0			0 (0)	0			1 (1)	1		
THINKING ABNORM	0 (0)	0			1 (<1)	1			1 (1)	1		
TREMOR	0 (0)	0			0 (0)	0			1 (1)	0		

[1]The term ALL RASH includes the following COSTART terms: RASH, RASH PUST, RASH MAC PAP, URTICARIA, STEVENS JOHNSON SYND and RASH VESIC BULL.

Includes adverse event data from studies 49,74,89 and 106 only.

Sex specific AEs used appropriate denominators. (In LTG group, N=228 and N=218 for male and female, respectively. In CBZ group, N=116 and N=131 for male and female, respectively. In PHT group, N= 54 and N= 41 for male and female, respectively.)

LAMICTAL Monotherapy NDA
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Table 6.28
Incidence of Adverse Experiences Leading to Discontinuation from Monotherapy Studies
in Newly Diagnosed Patients (Primary Study of Participation Only)

Body System Adverse Experience[1]	LAMICTAL (N=446) No. (%) of Pts	LAMICTAL (N=446) No. of Pts. with Maximum Intensity: Mild	Mod	Sev	CBZ (N=247) No. (%) of Pts	CBZ (N=247) No. of Pts. with Maximum Intensity: Mild	Mod	Sev	PHT (N= 95) No. (%) of Pts	PHT (N= 95) No. of Pts. with Maximum Intensity: Mild	Mod	Sev
Respiratory												
PHARYNGITIS	1 (<1)	0			0 (0)	0			0 (0)	0		
COUGH INC	0 (0)	0			1 (<1)	0			0 (0)	0		
DYSPNEA	0 (0)	0			1 (<1)	1			0 (0)	0		
EPISTAXIS	0 (0)	0			0 (0)	0			1 (1)	1		
LARYNGITIS	0 (0)	0			1 (<1)	0			0 (0)	0		
LUNG DISORDER	0 (0)	0			2 (<1)	2			0 (0)	0		
Skin												
ALL RASH	27 (6)	14			23 (9)	13			5 (5)	2		
RASH	20 (4)	11			21 (8)	11			5 (5)	2		
RASH MAC PAP	5 (1)	3			2 (<1)	2			0 (0)	0		
PRURITUS	2 (<1)	1			0 (0)	0			1 (1)	1		
SWEAT	2 (<1)	0			0 (0)	0			0 (0)	0		
URTICARIA	2 (<1)	0			0 (0)	0			0 (0)	0		
Special Senses												
DIPLOPIA	1 (<1)	0			1 (<1)	1			0 (0)	0		
HYPERACUSIS	1 (<1)	0			0 (0)	0			0 (0)	0		
TASTE PERVERS	1 (<1)	0			0 (0)	0			0 (0)	0		
EYE DISORDER	0 (0)	0			1 (<1)	0			0 (0)	0		
PAIN EYE	0 (0)	0			2 (<1)	1			0 (0)	0		
VISION ABNORM	0 (0)	0			1 (<1)	1			0 (0)	0		
Urogenital (Female)												
MENS DISORDER	0 (0)	0			1 (<1)	1			0 (0)	0		
METRORRHAGIA	0 (0)	0			1 (<1)	1			0 (0)	0		
PREGN UNINTEND	0 (0)	0			1 (<1)	0			0 (0)	0		

[1]The term ALL RASH includes the following COSTART terms: RASH, RASH PUST, RASH MAC PAP, URTICARIA, STEVENS JOHNSON SYND and RASH VESIC BULL.

Includes adverse event data from studies 49,74,89 and 106 only.

Sex specific AEs used appropriate denominators. (In LTG group, N=228 and N=218 for male and female, respectively. In CBZ group, N=116 and N=131 for male and female, respectively. In PHT group, N= 54 and N= 41 for male and female, respectively.)

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Table 7
Combined Center Summary of Demographic, Seizure History, and Presenting Seizure Characteristics Data

Parameter	Category/ Statistic	LAMICTAL	VPA
No. of Patients Randomized		76	80
Sex	Female	43(56.6%)	48(60.0%)
	Male	33(43.4%)	32(40.0%)
Race	Asian (Indian)	1(1.3%)	0(0.0%)
	Asian (Oriental)	1(1.3%)	0(0.0%)
	Black	8(10.5%)	11(13.8%)
	Other	14(18.4%)	14(17.5%)
	White	52(68.4%)	55(68.8%)
AED at Screen	Carbamazepine	48(63.2%)	46(57.5%)
	Phenytoin	28(36.8%)	34(42.5%)
Seizure Etiology	Idiopathic	52(68.4%)	49(61.3%)
	Symptomatic	24(31.6%)	31(38.8%)
Status Epilepticus?	Yes	7(9.2%)	7(8.8%)
	No	62(81.6%)	69(86.3%)
	Unknown	7(9.2%)	4(5.0%)
Presenting Seizure Type at Baseline[1]	Type A	31(40.8%)	35(43.8%)
	Type B	64(84.2%)	71(88.8%)
	Type C	38(50.0%)	27(33.8%)
Age (Yrs)	N	76	80
	Mean	36.9	36.0
	Std. Deviation	11.4	11.9
	Median	36	36
	Minimum		
	Maximum		
Weight (kg)	N	74	80
	Mean	78.3	70.4
	Std. Deviation	17.8	16.6
	Median	77.7	68.2
	Minimum		
	Maximum		
Height (cm)	N	76	80
	Mean	167.0	166.5
	Std. Deviation	9.9	14.0
	Median	166.3	167.6
	Minimum		
	Maximum		

[1] Multiple seizure types are possible within patient.

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Table 7
Combined Center Summary of Demographic, Seizure History, and Presenting Seizure Characteristics Data

Parameter	Category/ Statistic	LAMICTAL	VPA
Age at 1st Seizure (Yrs)	N	76	80
	Mean	14.5	15.5
	Std. Deviation	10.0	12.2
	Median	12	13
	Minimum		
	Maximum		
Duration of Epilepsy (Yrs)	N	76	80
	Mean	22.4	20.5
	Std. Deviation	10.9	11.0
	Median	22	20
	Minimum		
	Maximum		
Baseline Seizure Freq. (#/4weeks)	N	76	80
	Mean	27.2	18.7
	Std. Deviation	87.5	30.3
	Median	9	10
	Minimum		
	Maximum		
No. of Past AEDs	N	75	79
	Mean	4.4	4.6
	Std. Deviation	2.6	2.8
	Median	4	4
	Minimum		
	Maximum		

[1] Multiple seizure types are possible within patient.

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Table 11
Results of Per Protocol and Intent-to-Treat Analysis of Efficacy Data
Adjusted for Region

Study	Analysis	LAMICTAL No. Pts.	LAMICTAL No. Completers	LAMICTAL No. Failures	VPA No. Pts.	VPA No. Completers	VPA No. Failures	p-Value
Combined	Per Protocol	50	28 (56%)	22 (44%)	64	13 (20%)	51 (80%)	0.000
	Intent-to-Treat	76	28 (37%)	48 (63%)	80	13 (16%)	67 (84%)	0.003
	Intent-to-Treat/Worst Case	76	28 (37%)	48 (63%)	80	29 (36%)	51 (64%)	0.890
Study 030	Per Protocol	22	11 (50%)	11 (50%)	28	7 (25%)	21 (75%)	0.090
	Intent-to-Treat	31	11 (35%)	20 (65%)	35	7 (20%)	28 (80%)	0.179
	Intent-to-Treat/Worst Case	31	11 (35%)	20 (65%)	35	14 (40%)	21 (60%)	0.688
Study 031	Per Protocol	28	17 (61%)	11 (39%)	36	6 (17%)	30 (83%)	0.000
	Intent-to-Treat	45	17 (38%)	28 (62%)	45	6 (13%)	39 (87%)	0.002
	Intent-to-Treat/Worst Case	45	17 (38%)	28 (62%)	45	15 (33%)	30 (67%)	0.487

NOTES: In the Per Protocol Analysis, failure is defined as any patient who escaped. In the Intent-to-Treat Analysis, failure is defined as any patient who escaped or withdrew from the study.
In the Intent-to-Treat/Worst Case Analysis, for LTG patients, failure is defined as any patient who escaped or dropped out of the study. For VPA patients, Failure is defined as any patient who escaped.

Analysis is adjusted for Region.

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Table 18
Summary of Cumulative Treatment Failures
Per Protocol Analysis and Intent-to-Treat Analysis

Weeks from First Dose to Failure	Per Protocol Analysis		Intent-to-Treat Analysis	
	LAMICTAL (N=50)	VPA (N=64)	LAMICTAL (N=76)	VPA (N=80)
2	0 (0%)	0 (0%)	1 (1%)	0 (0%)
4	1 (2%)	3 (5%)	3 (4%)	5 (6%)
6	6 (12%)	11 (17%)	14 (18%)	15 (19%)
8	16 (32%)	32 (50%)	31 (41%)	39 (49%)
10	18 (36%)	37 (58%)	36 (47%)	46 (58%)
12	19 (38%)	44 (69%)	40 (53%)	53 (66%)
14	20 (40%)	48 (75%)	42 (55%)	58 (73%)
16	20 (40%)	49 (77%)	43 (57%)	61 (76%)
18	21 (42%)	50 (78%)	44 (58%)	64 (80%)
20	22 (44%)	51 (80%)	46 (61%)	67 (84%)
22	22 (44%)	51 (80%)	47 (62%)	67 (84%)
24	22 (44%)	51 (80%)	47 (62%)	67 (84%)
26	22 (44%)	51 (80%)	48 (63%)	67 (84%)

For the per protocol analysis, failure is defined as any patient who escaped.
For the intent-to-treat analysis, failure is defined as any patient who escaped or dropped out of the study.

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Table 19
Summary of Investigator's Global Evaluation Record
Per Protocol Analysis

Phase	Study Week	Trt	No. Pts.	Deterioration			Improvement				Analysis		
				Marked	Moderate	Mild	No Change	Mild	Moderate	Marked	Deterior	Improver	p-Value
T/Wk4	12	LTG	50	0 (0%)	2 (4%)	3 (6%)	16 (32%)	14 (28%)	13 (26%)	2 (4%)	5 (10%)	45 (90%)	0.919
		VPA	63	0 (0%)	2 (3%)	4 (6%)	20 (32%)	26 (41%)	9 (14%)	2 (3%)	6 (10%)	57 (90%)	
T/Wk8	16	LTG	46	0 (0%)	2 (4%)	11 (24%)	12 (26%)	8 (17%)	11 (24%)	2 (4%)	13 (28%)	33 (72%)	0.138
		VPA	57	1 (2%)	12 (21%)	11 (19%)	9 (16%)	14 (25%)	8 (14%)	2 (4%)	24 (42%)	33 (58%)	
M/Wk4	20	LTG	35	1 (3%)	1 (3%)	1 (3%)	5 (14%)	13 (37%)	7 (20%)	7 (20%)	3 (9%)	32 (91%)	0.095
		VPA	27	0 (0%)	4 (15%)	3 (11%)	6 (22%)	7 (26%)	3 (11%)	4 (15%)	7 (26%)	20 (74%)	
M/Wk8	24	LTG	29	0 (0%)	0 (0%)	0 (0%)	8 (28%)	6 (21%)	8 (28%)	7 (24%)	0 (0%)	29 (100%)	0.186
		VPA	15	0 (0%)	0 (0%)	1 (7%)	4 (27%)	5 (33%)	2 (13%)	3 (20%)	1 (7%)	14 (93%)	
M/Wk12	28	LTG	31	0 (0%)	1 (3%)	2 (6%)	9 (29%)	7 (23%)	7 (23%)	5 (16%)	3 (10%)	28 (90%)	0.861
		VPA	15	0 (0%)	0 (0%)	1 (7%)	4 (27%)	3 (20%)	4 (27%)	3 (20%)	1 (7%)	14 (93%)	
F/Taper	30	LTG	31	0 (0%)	3 (10%)	6 (19%)	12 (39%)	3 (10%)	6 (19%)	1 (3%)	9 (29%)	22 (71%)	0.998
		VPA	45	0 (0%)	6 (13%)	6 (13%)	24 (53%)	7 (16%)	2 (4%)	0 (0%)	12 (27%)	33 (73%)	
F/No Drug	31	LTG	33	0 (0%)	4 (12%)	5 (15%)	13 (39%)	4 (12%)	6 (18%)	1 (3%)	9 (27%)	24 (73%)	0.866
		VPA	52	1 (2%)	8 (15%)	6 (12%)	22 (42%)	11 (21%)	2 (4%)	2 (4%)	15 (29%)	37 (71%)	

NOTE: p-Values, adjusting for region, measure the level of association between deterioration/improvement and treatment. All subcategories of deterioration are grouped to comprise the deterioration category.
All subcategories of improvement as well as 'No Change' are grouped to comprise the improvement category.

PHASE: T=Transition, M=Monotherapy, F=Follow-Up. Post '/' indicates specific timepoint within phase.

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Table 20
Summary of Investigator's Global Evaluation Record
Intent-to-Treat Analysis

Phase	Study Week	Trt	No. Pts.	Deterioration			Improvement				Analysis		
				Marked	Moderate	Mild	No Change	Mild	Moderate	Marked	Deterior	Improver	p-Value
T/Wk4	12	LTG	65	0 (0%)	5 (8%)	6 (9%)	20 (31%)	18 (28%)	14 (22%)	2 (3%)	11 (17%)	54 (83%)	0.117
		VPA	73	0 (0%)	2 (3%)	4 (5%)	25 (34%)	28 (38%)	11 (15%)	3 (4%)	6 (8%)	67 (92%)	
T/Wk8	16	LTG	53	0 (0%)	2 (4%)	13 (25%)	14 (26%)	9 (17%)	13 (25%)	2 (4%)	15 (28%)	38 (72%)	0.232
		VPA	65	1 (2%)	13 (20%)	11 (17%)	12 (18%)	16 (25%)	9 (14%)	3 (5%)	25 (38%)	40 (62%)	
M/Wk4	20	LTG	40	1 (3%)	1 (3%)	2 (5%)	5 (13%)	16 (40%)	8 (20%)	7 (18%)	4 (10%)	36 (90%)	0.127
		VPA	31	0 (0%)	4 (13%)	4 (13%)	7 (23%)	9 (29%)	3 (10%)	4 (13%)	8 (26%)	23 (74%)	
M/Wk8	24	LTG	29	0 (0%)	0 (0%)	0 (0%)	8 (28%)	6 (21%)	8 (28%)	7 (24%)	0 (0%)	29 (100%)	0.186
		VPA	15	0 (0%)	0 (0%)	1 (7%)	4 (27%)	5 (33%)	2 (13%)	3 (20%)	1 (7%)	14 (93%)	
M/Wk12	28	LTG	31	0 (0%)	1 (3%)	2 (6%)	9 (29%)	7 (23%)	7 (23%)	5 (16%)	3 (10%)	28 (90%)	0.861
		VPA	15	0 (0%)	0 (0%)	1 (7%)	4 (27%)	3 (20%)	4 (27%)	3 (20%)	1 (7%)	14 (93%)	
F/Taper	30	LTG	40	0 (0%)	4 (10%)	9 (23%)	15 (38%)	5 (13%)	6 (15%)	1 (3%)	13 (33%)	27 (68%)	0.823
		VPA	52	1 (2%)	6 (12%)	7 (13%)	27 (52%)	9 (17%)	2 (4%)	0 (0%)	14 (27%)	38 (73%)	
F/No Drug	31	LTG	56	0 (0%)	6 (11%)	12 (21%)	21 (38%)	8 (14%)	8 (14%)	1 (2%)	18 (32%)	38 (68%)	0.787
		VPA	64	1 (2%)	9 (14%)	12 (19%)	27 (42%)	11 (17%)	2 (3%)	2 (3%)	22 (34%)	42 (66%)	

NOTE: p-Values, adjusting for region, measure the level of association between deterioration/improvement and treatment. All subcategories of deterioration are grouped to comprise the deterioration category.
All subcategories of improvement as well as 'No Change' are grouped to comprise the improvement category.

PHASE: T=Transition, M=Monotherapy, F=Follow-Up. Post '/' indicates specific timepoint within phase.

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Table 23
Results of Per Protocol and Intent-to-Treat Subgroup Analysis of Efficacy Data

Analysis	Strata	Category	LAMICTAL No. Pts.	LAMICTAL No. Completers	LAMICTAL No. Failures	VPA No. Pts.	VPA No. Completers	VPA No. Failures	p-Value (Adjusted for Region and Strata)	p-Value (Breslow-Day)
Per Protocol	Age	13-<18	3	2 (67%)	1 (33%)	2	0 (0%)	2 (100%)	0.000	0.201
		18-59	46	25 (54%)	21 (46%)	59	13 (22%)	46 (78%)		
		>59	1	1 (100%)	0 (0%)	3	0 (0%)	3 (100%)		
	Baseline AED	CBZ	30	20 (67%)	10 (33%)	39	8 (21%)	31 (79%)	0.000	0.290
		PHT	20	8 (40%)	12 (60%)	25	5 (20%)	20 (80%)		
	Race	Other	18	11 (61%)	7 (39%)	18	5 (28%)	13 (72%)	0.000	0.258
		White	32	17 (53%)	15 (47%)	46	8 (17%)	38 (83%)		
	Sex	Female	25	14 (56%)	11 (44%)	40	9 (23%)	31 (78%)	0.000	0.445
		Male	25	14 (56%)	11 (44%)	24	4 (17%)	20 (83%)		
Intent-to-Treat	Age	13-<18	5	2 (40%)	3 (60%)	2	0 (0%)	2 (100%)	0.005	0.204
		18-59	68	25 (37%)	43 (63%)	74	13 (18%)	61 (82%)		
		>59	3	1 (33%)	2 (67%)	4	0 (0%)	4 (100%)		
	Baseline AED	CBZ	48	20 (42%)	28 (58%)	46	8 (17%)	38 (83%)	0.003	0.669
		PHT	28	8 (29%)	20 (71%)	34	5 (15%)	29 (85%)		
	Race	Other	24	11 (46%)	13 (54%)	25	5 (20%)	20 (80%)	0.005	0.410
		White	52	17 (33%)	35 (67%)	55	8 (15%)	47 (85%)		
	Sex	Female	43	14 (33%)	29 (67%)	48	9 (19%)	39 (81%)	0.003	0.221
		Male	33	14 (42%)	19 (58%)	32	4 (13%)	28 (88%)		
Intent-to-Treat/WC	Age	13-<18	5	2 (40%)	3 (60%)	2	0 (0%)	2 (100%)	0.999	0.070
		18-59	68	25 (37%)	43 (63%)	74	28 (38%)	46 (62%)		
		>59	3	1 (33%)	2 (67%)	4	1 (25%)	3 (75%)		
	Baseline AED	CBZ	48	20 (42%)	28 (58%)	46	15 (33%)	31 (67%)	0.801	0.128
		PHT	28	8 (29%)	20 (71%)	34	14 (41%)	20 (59%)		
	Race	Other	24	11 (46%)	13 (54%)	25	12 (48%)	13 (52%)	0.878	0.027

NOTES: In the Per Protocol Analysis, failure is defined as any patient who escaped. In the Intent-to-Treat Analysis, failure is defined as any patient who escaped or withdrew from the study.
In the Intent-to-Treat/Worst Case Analysis, for LTG patients, failure is defined as any patient who escaped or dropped out of the study. For VPA patients, Failure is defined as any patient who escaped.

p-Values are adjusted for region and strata.

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Table 23
Results of Per Protocol and Intent-to-Treat Subgroup Analysis of Efficacy Data

Analysis	Strata	Category	LAMICTAL No. Pts.	LAMICTAL No. Completers	LAMICTAL No. Failures	VPA No. Pts.	VPA No. Completers	VPA No. Failures	p-Value (Adjusted for Region and Strata)	p-Value (Breslow-Day)
Intent-to-Treat/WC	Race	White	52	17 (33%)	35 (67%)	55	17 (31%)	38 (69%)		
	Sex	Female	43	14 (33%)	29 (67%)	48	17 (35%)	31 (65%)		
		Male	33	14 (42%)	19 (58%)	32	12 (38%)	20 (63%)	0.867	0.165

NOTES: In the Per Protocol Analysis, failure is defined as any patient who escaped. In the Intent-to-Treat Analysis, failure is defined as any patient who escaped or withdrew from the study.
In the Intent-to-Treat/Worst Case Analysis, for LTG patients, failure is defined as any patient who escaped or dropped out of the study. For VPA patients, Failure is defined as any patient who escaped.

p-Values are adjusted for region and strata.